

Application No.: 10/562,089
Attorney Docket No.: 47675-066US0
First Applicant's Name: Catherine Lofton-Day
Application Filing Date: January 28, 2008
Date of Restriction Requirement: November 16, 2009
Date of Response: March 16, 2010
Examiner: Sarae L. Bausch

REMARKS

Claims 1-22 are pending and have been subjected to restriction by the Examiner.

Claims 2, 3, and 23 have been cancelled without prejudice herein.

Claims 1, 4, 5, 7, 8, 11-14, 18, and 20-22 have been amended herein to conform with the Restriction Requirement and Applicants' elections and otherwise to conform with U.S. practice. Additionally, support for the recitation of "or metastasis" in claims 4, 5, and 8 can be found throughout the originally-filed specification.

New claim 24, fully supported by the originally-filed specification (e.g., at paragraphs [0161] and [0162]), has been added. No new matter has been added.

Initial Group election

The Examiner, by way of restrictions, is requesting an initial election of one Group of claims from among Groups I-II as described in the Restriction Requirement:

Applicants herein elect Group I (claims 1-5 and 8-21, drawn to a method of detecting cell proliferative disorders by methylation) *with traverse*.

Further election of specific combination of genes

Additionally, the Examiner has requested election of a specific gene or gene combination and their associated SEQ ID NOs to which the claims will be limited as described in the Restriction Requirement:

Applicants herein elect the following combination, with traverse:

"ALX4" and its SEQ ID NO:2 and

"TPEF" and its SEQ ID NO:3.

The basis of Applicants' traversal is three-fold.

Application No.: 10/562,089
Attorney Docket No.: 47675-066US0
First Applicant's Name: Catherine Lofton-Day
Application Filing Date: January 28, 2008
Date of Restriction Requirement: November 16, 2009
Date of Response: March 16, 2010
Examiner: Sarae L. Bausch

First, Applicants contend that the bisulfite treated sequences SEQ ID NOS:7, 8, 15, and 16, corresponding to genomic SEQ ID NO:2 should be included for examination along with SEQ ID NO:2, and additionally that the bisulfite treated sequences SEQ ID NOS:9, 10, 17, and 18 corresponding to genomic SEQ ID NO:3 should be included for examination along with SEQ ID NO:3. As can be seen in Table 2 at page 18 of the specification and the Sequence Listing, SEQ ID NOS:7, 8, 15, and 16 correspond to chemically-treated (bisulfite) versions of SEQ ID NO:2, wherein SEQ ID NOS:7 (sense) and 8 (antisense) correspond to treated sequences wherein the CpG dinucleotides of SEQ ID NO:2 are methylated, and wherein SEQ ID NOS:15 (sense) and 16 (antisense) correspond to treated sequences wherein the CpG dinucleotides of SEQ ID NO:2 are unmethylated. Likewise, SEQ ID NOS:9, 10, 17, and 18 correspond to chemically-treated (bisulfite) versions of SEQ ID NO:3, wherein SEQ ID NOS:9 (sense) and 10 (antisense) correspond to treated sequences wherein the CpG dinucleotides of SEQ ID NO:3 are methylated, and wherein SEQ ID NOS:17 (sense) and 18 (antisense) correspond to treated sequences wherein the CpG dinucleotides of SEQ ID NO:3 are unmethylated. The elected claims should, therefore, not only be examined with respect to SEQ ID NOS:2 and 3, but additionally with respect to each of SEQ ID NOS:7, 8, 9, 10, 15, 16, 17 and 18, because they correspond to bisulfite-treated sequences for the identical sequence regions of genomic SEQ ID NOS:2 and 3, and the patentability of claims limited by these SEQ ID NOS will be determined based on the novelty of analysis based on the two genomic sequence regions SEQ ID NOS:2 and 3 for the claimed indications. Applicants point out that it has been the consistent practice of the Office to include the bisulfite-converted sequences along with the corresponding genomic sequence(s) for purposes of examination.

Second, Applicants respectfully request that claim 4, which recites one member (ALX4) of the elected combination (ALX4 and TPEF), be included in the elected group, as searching this claim

Application No.: 10/562,089
Attorney Docket No.: 47675-066US0
First Applicant's Name: Catherine Lofton-Day
Application Filing Date: January 28, 2008
Date of Restriction Requirement: November 16, 2009
Date of Response: March 16, 2010
Examiner: Sarae L. Bausch

does not represent a significant additional burden on the Office in view of the fact that ALX4 must be searched in the context of searching the elected combination (ALX4 and TPEF).

Third, with respect to the election as between Groups I and II, this application was filed in accordance with 35 U.S.C. §371, and while national stage applications of international applications are similar to national applications (MPEP 201), there are differences such as the inapplicability of restriction practice to national stage applications. Restriction practice is applied to national applications, whereas *unity of invention* practice is applied to national stage applications (MPEP 1800).

The Examiner asserts that the special technical feature of group I is considered to be TIMP3 and DAPK genes and that Ester et al. teaches promoter hypermethylation changes in APC, p16INK4a, DAPK and TIMP3 and teaches that those genes are methylated in colon cancer. The Examiner further asserts that the technical feature linking the recited groups I-II does not constitute a special technical feature as defined by PCT rule 13.2, because it does not define a contribution over the prior art.

Applicants have herein elected ALX4 and TPEF (SEQ ID NOS:2 and 3) as the specific combination of genes and their associated bisulfite-converted sequences (SEQ ID NOS:7, 8, 9, 10, 15, 16, 17, and 18), and none of the aforementioned genes (e.g. APC, p16INK4a, DAPK and TIMP3) are included in the election. Claims in Group I (encompassed by claims 1-5, 8-21) are drawn to a method of detecting cell proliferative disorders using the methylation status of ALX4 and TPEF (SEQ ID NOS:2 and 3), and in particular claims, use of the bisulfite-converted sequences SEQ ID NOS:2, 3, 7, 8, 9, 10, 15, 16, 17 and 18. Claims in Group II (encompassed by claims 6, 7 and 22) are directed to nucleic acids of SEQ ID NOS:7, 8, 9, 10, 15, 16, 17 and 18 (claims 6 and 7) and a kit utilizing same (claim 22). Thus, the subject matter of most of the claims of Groups 1 and

Application No.: 10/562,089
Attorney Docket No.: 47675-066US0
First Applicant's Name: Catherine Lofton-Day
Application Filing Date: January 28, 2008
Date of Restriction Requirement: November 16, 2009
Date of Response: March 16, 2010
Examiner: Sarae L. Bausch

2 are linked as they share a common special technical feature of the bisulfite-converted sequences
SEQ ID NOS:7, 8, 9, 10, 15, 16, 17, and 18.

Applicants therefore additionally request that Group II be included with the elected Group I
for Examination.

Application No.: 10/562,089
Attorney Docket No.: 47675-066US0
First Applicant's Name: Catherine Lofton-Day
Application Filing Date: January 28, 2008
Date of Restriction Requirement: November 16, 2009
Date of Response: March 16, 2010
Examiner: Sarae L. Bausch

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request entry of the present Response and Amendment provided herein. The Examiner is encouraged to phone Applicants' attorney, Barry L. Davison, to resolve any outstanding issues and expedite allowance of this application.

Davis Wright Tremaine LLP
1201 Third Avenue, Suite 2200
Seattle, Washington 98101-3045
Telephone: 206-757-8023
Facsimile: 206-757-7700

Respectfully submitted,
Catherine Lofton-Day et al.
Davis Wright Tremaine LLP

/Barry L. Davison, Ph.D., J.D./
Barry L. Davison, Ph.D., J.D.
Attorney for Applicants
Registration No. 47,309